REMARKS

Claims 39-47 and 49-55 are pending and claim48 has been canceled without prejudice. Applicants expressly reserve the right to pursue the canceled subject matter in this application or subsequent applications that claim the benefit of this application.

Applicants have amended claim 39 to specify a monoclonal antibody or antigen-binding fragment. The amended claims are fully supported by the specification (e.g., page 3, lines 13-17) and originally filed claim 12.

Applicants have amended claims 40, 46-47 and 52 to improve their form and to more particularly point out the claimed invention. The amended claims are fully supported by the specification (e.g., page 16, lines 20-29) and originally filed claims.

Applicants have amended claims 41 and 49-50 to improve their form and to more particularly point out the claimed invention. The amended claims are fully supported by the specification and originally filed claims.

Applicants have amended claim 55 to improve its form and to specify "a known T-cell epitope derived from a different protein" and "produced by said hybrid cell". The amended claims are fully supported by the specification (e.g., page 24, lines 6-8 and page 24, lines 28-30) and originally filed claim 34.

No new matter has been introduced. Applicants respectfully request reconsideration in view of the following remarks. The Examiner's rejections and comments are addressed below in the order they were raised in the Office Action.

DETAILED ACTION

Applicants note with appreciation that the responses filed April 13, 2007 and April 19, 2007 have been entered.

Objections to the Specification

1. The Examiner has objected to imbedded active hyperlinks on page 14. The Examiner also suggests that "cytochrome" was intended on page 24, line 7 and "avenue" was intended on page 26, line 11. Applicants have amended the specification to delete "http://" and corrected the typographical errors as suggested by the Examiner.

Claim Rejections under 35 U.S.C. § 112, first paragraph

2. The Examiner has objected to the specification and claim 40 as allegedly failing to provide an adequate written description and failing to provide an enabling disclosure. The Examiner argues that the specification does not provide evidence that the claimed biological materials are (1) known; (2) reproducible form the written description; or (3) deposited in compliance with the criteria set forth in37 CFR §§ 1.801-1.809. Specifically, the claim allegedly requires the 3B10, 4B2, 10, 17, 24, 25, 26, 27, 31, 41, 50, 60, 87, 3-4A, and 3-11F antibodies.

Applicants request that this objection be held in abeyance. An acceptable deposit of the hybridomas will be made before the date of payment of the issue fee.

3. The Examiner has objected to the specification and claims 39-51 and 53-55 as allegedly failing to provide an adequate written description and failing to provide an enabling disclosure. The Examiner argues that the specification does not provide evidence that the claimed biological materials are (1) known; (2) reproducible form the written description; or (3) deposited in compliance with the criteria set forth in37 CFR §§ 1.801-1.809. Specifically, the claim allegedly requires the AL1 and either AL12 or AL13 antibodies.

Applicants request that this objection also be held in abeyance. An acceptable deposit of the hybridomas will be made before the date of payment of the issue fee.

4. Claims 40, 46, 47, and 52 are rejected under 35 USC §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and was not described in the specification in such

a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate with that as claimed.

Applicants respectfully disagree. However, in an effort to expedite prosecution of the application, the claims have been amended and the amendment is believed to obviate the rejection. In particular, the claims have been amended to specify that the claimed antibodies, or antigen binding fragments thereof, comprise a complete complement of 6 CDRs (e.g., heavy chain CDR1, CDR2, and CDR3 and light chain CDR1, CDR2, and CDR3).

The Office Action states that "Applicants have reduced to practice and taught as functional in the invention only intact variable antibody chains as disclosed, such as SEQ ID NOs 3 and 8, with the CDRs at specific regions of the chains and both such heavy and light chains forming the functional antibody." Applicants respectfully disagree and submit that such a standard, e.g., that only a single antibody having six specifically defined CDR sequences may be claimed, is clearly inconsistent with the written description guidelines. Example 16 of the Revised Interim Written Description Guidelines Training Materials (the "Guidelines"), states that:

> Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum, of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Accordingly, as long as a fully characterized antigen is disclosed, the specification is sufficient to provide written description support for claims directed to antibodies that bind the antigen even if no antibodies were actually made. In particular, such a disclosure provides written description for the full range of antibodies that bind to that antigen without any sort of sequence limitation. In Example 16, a "fully characterized antigen" is deemed to be provided upon disclosure of (i) isolation of the antigen, (ii) molecular weight of the antigen, and (iii) a method for purification of the antigen. Using this standard, the instant application clearly meets the standard for adequate written description. The instant application describes the discovery of a type III epitope of PTN, a method for determining for isolating antibodies to it, and actual reduction to practice of a number of antibodies that bind to a type III epitope of PTN, including 3B10. (see e.g., paragraph [0187] of the published application). The CDR sequences for 3B10 are also provided. Accordingly, one of skill

in the art reading the specification would clearly have understood that Applicants were in possession of the full scope of the instant claims.

Based on the remarks above, Applicants submit that the instant application clearly provides adequate support for the full scope of antibodies that bind a type III epitope of PTN. Applicants submit that since the full complement of antibodies to a type III epitope of PTN are adequately supported by the instant application, the claimed subgenus of antibodies is also clearly supported by the specification. In particular, the Examiner's attention is directed to Example 14 of the Guidelines. Example 14 explains that claims to protein variants (which includes variants having substitutions, deletions, insertions and additions) having a common structural feature (e.g., 95% identical to SEQ ID NO: 3 in the example) and a specified function find adequate written description support in a specification which discloses (i) that procedures for making variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions is routine in the art and (ii) an assay for detecting the claimed activity, *even when no examples of variants are actually provided.* Based on this standard, the instant application clearly meets the written description standard for the instant claims. In particular, the claims are directed to a particular subset of antibodies, or antigen binding fragments thereof to a type III epitope of PTN, having a common structural feature (e.g., a heavy chain or light chain comprising a sequence selected from SEQ ID NOs:3, 5, 6, 7, 8, 10, 11, and 12 and a specified function, e.g., binding to a type III epitope of PTN. Furthermore, the specification discloses a variety of well known art recognized methods for producing antibodies. The Guidelines in Example 16 specifically state that production of antibodies is mature technology and the level of skill is high and advanced. Accordingly, the application clearly meets the requirements for an adequate written description as provided in the Guidelines.

Therefore, in view of Examples 14 and 16 of the Guidelines and the extensive description and working examples provided in the specification, Applicants have clearly provided sufficient written description for the instant claims. The claims cover a structurally well characterized class of proteins (e.g., antibodies) and the specification provides assays for identifying all of the antibodies which have the specified activity. Furthermore, Applicants provide at least one working example that is representative of the claimed genus. Accordingly, one of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by the members of the genus.

The Office Action alleges that the specification does not reasonably provide enablement for making and using antibodies or antigen-binding fragments that do not comprise all six CDRs. Applicants respectfully disagree with the rejection. However, in an effort to expedite prosecution of the application, the claims have been amended and the amendments are believed to obviate the rejection. In particular, claims 40, 46 and 47 as amended are directed, at least in part, to an antibody or an antigen binding fragment thereof that comprises the full complement of 6 CDRs and binds to a type III epitope of PTN. Applicants submit that the specification clearly enables such claims. In particular, the specification provides extensive teachings of how to produce and screen for a monoclonal antibodies that bind to a type III epitope of PTN (see e.g., paragraph [0187] of the published application). Accordingly, Applicants submit that the specification clearly is sufficient to enable one of ordinary skill in the art to make and use the claimed invention without undue experimentation. With regards to the biological deposits, applicants request that this rejection be held in abeyance. An acceptable deposit will be made before the date of payment of the issue fee. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 112, second paragraph

5. Claims 39-55 are rejected under 35 USC 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that claim 39 and claims dependent thereupon, "The" antibody or fragment lacks antecedent basis and that it is not clear what applicant intends as encompassed by a "type III epitope" or a "biological activity". Applicants respectfully traverse.

Applicants have amended "The" to "A" thus obviating the antecedent basis rejection.

The terms a "type III epitope" or a "biological activity" are described in the specification in such a way as to be clear to one of ordinary skill in the art. Specifically, a "type III epitope" is defined as an epitope of PTN that is different than the epitopes of AL1, AL12 and AL13 (see page 18, lines 5-12). A "biological activity" is described in the therapeutic uses section of the specification (see pages 27-32). Each of the activities described in this section is a biological activity of PTN.

One of ordinary skill in the art would understand what is meant by each of these terms based on the description in the specification. MPEP 2111.01 (iv) states,

> Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings").

Accordingly, it is urged that claim 39 is definite and reconsideration and withdrawal of this rejection are respectfully requested.

6. The Examiner alleges that claim 40 is vague in the absence of recitation of deposit accession numbers to clearly identify the claimed antibody/hybridoma species and that "the same epitope" lacks antecedent basis and it is unclear what is within the metes and bounds of the invention because it is not clear what applicant intends as encompassed by "substantially" the same epitope. The Examiner further alleges that improper Markush language is used in alternative (c). Applicants respectfully traverse.

Applicants request that the recitation of deposit accession number be held in abeyance as discussed *supra*. An acceptable deposit will be made before the date of payment of the issue fee.

Applicants have amended the Markush group language thereby obviating this aspect of the rejection.

Applicants do not believe there is an antecedent basis problem with the recited phrase as it refers to the epitope described subsequently. Nevertheless, solely to expedite prosecution, applicants have amended "substantially the same" to "an epitope, which is substantially the same as an epitope of the monoclonal antibody".

With regards to the meaning of the term "substantially" the MPEP 2173.05(b) states:

> The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.

Applicants respectfully remind the Examiner that according to the MPEP claim language that is acceptable if one of ordinary skill in the art would be able to understand what is claimed in light of the specification. Here the specification provides sufficient guidance to one of ordinary skill for interpreting the claims. The term "substantially the same epitope" as used in claim 40 is clearly defined in the specification as when "amino acid mutations in the protein that reduce or eliminate binding of one antibody also reduce or eliminate binding of the other antibody, and/or if the antibodies compete for binding to the protein, i.e., binding of one antibody to the protein reduces or eliminates binding of the other antibody" (see page 8, lines 10-23). The specification further provides methods of making this analysis such as a competition assay. As required by the MPEP, in light of the specification, one of ordinary skill in the art would understand the claimed subject matter.

This standpoint is further consistent with the same MPEP section, which particularly listed the use of the word "substantially" as being definite if a skilled artisan would be reasonably apprised of the meaning of the term, especially in view of the guidelines set forth in the specification. *See, In re Nehrenberg*, 280 F.2d 161, 126 USPQ 383 (CCPA 1960). In *In re Mattison*, the court held that the limitation 'to substantially increase the efficiency of the compound as a copper extractant' was definite in view of the general guidelines contained in the specification. *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). A similar result was also seen in *Andrew Corp. v. Gabriel Electronics*, 847 F.2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988), where the Court held that the limitation 'which produces substantially equal E and H plane illumination patterns' was definite because one of ordinary skill in the art would know what was meant by 'substantially equal.' It is Applicants position, that in this case, the term substantially is being used consistent with the usage in *Mattison* and *Andrew Corp.* Accordingly, it is urged that claim 40 is definite and reconsideration and withdrawal of this rejection are respectfully requested.

7. The Examiner alleges that claims 41, 46, 47, 49, 50 and 52 contain improper Markush language. Applicants have amended the claims thereby obviating the rejection.

8. The Examiner alleges that in claims 42-45, it is not clear what is being further limited other than intended use of the antibody. Applicants respectfully traverse.

Applicants disagree that the "functional language" in these claims are merely intended use and do not limit the claim. Claims 42-45 are directed to antibodies or antigen-binding fragments thereof that inhibit cancer growth, cell proliferation, metastasis, or angiogenesis. These claims are further limiting than independent claim 39 which encompasses antibodies which may not necessarily have the desired functions. The Courts have consistently ruled that functional language can be used to further define the claimed invention. See, e.g., footnote 3 in *Haberman v. Gerber Products Co.*, Slip Copy, 2007 (WL 1577970 (Fed. Cir. 2007) in which in response to an argument that certain functional language was merely intended use the court stated: "We are not persuaded by Gerber's argument that this language is a statement of intended use which does not limit the claim." Accordingly, it is urged that claims 42-45 are definite and reconsideration and withdrawal of this rejection are respectfully requested.

9. The Examiner alleges that in claim 55, "said" protein lacks antecedent basis and that the interrelationship of the steps in the method of production are not clear because there is no connection between the step of isolating a monoclonal antibody and any of the other steps. Applicants have amended the claim from "said" to "a" protein thus obviating the lack of antecedent basis rejection. Applicants have amended the claim to add "produced by said hybrid cell", thus obviating the rejection that there is no connection between the steps of isolating a monoclonal antibody and any of the other steps (see page 24, lines 28-30). Accordingly, it is urged that claim 55 is definite and reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 102

10. The Examiner has rejected claims 39-46, 49, 50, 53 and 54 under 35 U.S.C. 102(b) as allegedly being anticipated by Jäger et al. (Int. J. Cancer 73: 537, 1997). Jäger et al. allegedly teach an antibody to PTN which inhibits the biological activity of the protein. The Examiner argues that the antibody binds to at least one epitope as instantly defined. Applicants respectfully traverse.

Applicants disagree, nevertheless, solely in order to expedite prosecution, claim 39 has been amended to recite "monoclonal" antibody or antigen-binding fragment thereof. The remaining rejected claims depend directly or indirectly from these claims. Jäger et al. do not teach monoclonal antibodies.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). "The identical invention must be shown in as complete detail as is contained in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, Jäger et al. do not contain every element of the instant claims. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b) are respectfully requested.

11. The Examiner has rejected claim 52 under 35 U.S.C. 102(e)(2) as allegedly being anticipated by Büdingen et al. (US Patent 6,569,431). Büdingen et al allegedly teach a sequence SEQ ID NO:8 which comprises SEQ ID NO:12 of the instant claim. Applicants respectfully traverse.

Applicants disagree, nevertheless, solely in order to expedite prosecution, claim 52 has been amended to delete SEQ ID NO: 12. Büdingen et al. do not teach the remaining sequences. Therefore, Büdingen et al. do not contain every element of the instant claims. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e)(2) are respectfully requested.

12. Claim 55 is rejected under 35 U.S.C. §102(e)(2) as allegedly being anticipated by Paliard et al. (US Patent 6,562,346). Paliard et al allegedly teach the elicitation of monoclonal antibodies by immunization of a mammal with fusion proteins comprising a protein of interest and at least one T cell epitope, hybridization of B cells obtained from the immunized animal to a myeloma cell, and identification and culture of relevant hybridomas. Applicants respectfully traverse.

Applicants disagree, nevertheless, solely in order to expedite prosecution, claim 55 has been amended to recite "a known T-cell epitope derived from a different protein". Paliard et al. only teach a T-cell epitope from the same protein and not one derived from a different protein than the remaining part of the fusion. Therefore, Paliard et al. do not contain every element of the instant claims. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e)(2) are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants believe no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. GUH-026-101 from which the undersigned is authorized to draw.

Dated: January 16, 2008

Respectfully submitted,

By _____

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